

REMARKS

Upon entry of the present amendments, claims 3-25 and 28-30 are pending in this application. Non-elected claims 1-2 and 26-27 are canceled without prejudice. Claims 3, 8, 14, 16, 17, 19, 22, 23, 24, 28 and 30 were amended as shown above. Applicants reserve the right to pursue all canceled subject matter in one or more continuation, divisional, or continuation-in-part applications. No new matter has been added. For the reasons that follow, it is believed that the claims are in condition for allowance.

THE REJECTION UNDER 35 U.S.C. § 112, SECOND PARAGRAPH SHOULD BE WITHDRAWN

Claims 3-25 and 28-30 were rejected under 35 U.S.C. § 112, second paragraph, as allegedly indefinite for the reasons set forth on pages 2-5 of the Office Action. Specifically, the Examiner alleges that the phrase “surface comprises a region defined by at least some of the functional additive” is uncertain as to meaning and scope and that the term “functional additive” is uncertain. Applicants respectfully submit that the phrase “surface comprises a region defined by at least some of the functional additive” is not uncertain. The specification discloses that “[b]ecause porous substrates of the invention are made of a porous polymeric matrix into which inclusions of functional additive are trapped, a surface of a typical substrate will contain regions of functional additive surrounded by regions of the polymeric matrix.” Specification, page 14, lines 1-3. The specification further discloses that “[i]n a typical substrate of the invention, functional additive covers about 5% to about 60%, and more typically of about 10% to about 50% of the surface area of the substrate.” Specification, page 14, lines 6-8. Furthermore, Figure 1 shows a “defined” surface region created by the functional additive on the surface. Thus, one of ordinary skill in the art reading the phrase “surface comprises a region defined by at least some of the functional additive” would readily understand its meaning and scope. Because it is a well-established principle of patent law that the meaning of the claims is to be interpreted in light of the specification, Applicants respectfully submit that the scope of above-mentioned term is particularly and clearly recited. Manual of Patent Examining Procedure (M.P.E.P.) § 2173.05(a), citing *In re Zletz*, 893 F.2d 319 (Fed. Cir. 1989).

Regarding the term “functional additive,” Applicants respectfully submit that the term is not uncertain, as it is defined in the specification as “materials that contain functional groups to which biological and/or chemical moieties can be covalently attached.”

Specification, page 10, lines 16-18. The specification provides further meaning and scope to the term “functional additive” by listing examples of both functional additives and functional groups. Specification, page 3, lines 13-21. Since the meaning of the claims is to be interpreted in light of the specification, Applicants respectfully submit that the scope of above-mentioned term is particularly and clearly recited. M.P.E.P. § 2173.05(a). For these reasons, Applicants submit that this rejection be withdrawn.

The Examiner alleges that claim 8 is confusing and unclear because it recites a specific polymer in line 2 in parenthesis after “ketone.” Claim 8 has been amended to correct this typographical error. Support for this amendment can be found in the specification on page 12, lines 19-21.

The Examiner alleges that in claim 13 and other, unspecified related claims the relationship of the spacer and biological and chemical moiety to the functional additive is unclear. Applicants note that, as recited in claim 3, the spacer is covalently bound to the region defined by at least some of the functional additive, and the biological or chemical moiety is covalently or noncovalently bound to the spacer. The specification discusses this relationship in great detail. *See e.g.*, Specification, page 2, lines 28-31. Thus, one of ordinary skill in the art would readily understand the relationship of the spacer and the biological and chemical moiety to the functional additives. M.P.E.P. § 2173.05(a). For this reason, Applicants submit that this rejection be withdrawn.

The Examiner alleges that claim 14 is confusing because it indirectly depends from claim 3 and, unlike claim 3, requires that the porous substrate and biological or chemical moiety be attached to the spacer. Claim 14 has been amended to avoid confusion. Support for this amendment can be found on page 4, lines 1-5 of the specification.

The Examiner alleges that in line 4 of claim 14 and line 3 of claim 17, R and R' are defined, but Formula I does not contain R and R'. Applicants have amended claims 14 and 17 to replace R and R' with R¹ and R². Support for this amendment can be found on page 4, line 2 of the specification.

The Examiner alleges that the form of R³ is uncertain in line 5 of claim 16, line 4 of claim 17, and line 8 of claim 22. Although Applicants respectfully disagree, claims 14, 16, 17, 22 and 23 have been amended to further their prosecution. Support for the amendments can be found in the specification on page 4, line 3; page 4, line 17; and page 6, line 12.

The Examiner alleges that in claim 17 the relationship of the spacer to the substrate and functional additive is unclear. Although Applicants respectfully disagree, claim

17 has been amended to recite that the spacer of Formula I is covalently attached to at least a portion of the functional additive and to a chemical or biological moiety. Support for this amendment can be found in the specification. Specification, page 4, line 22 - page 5, line 2.

The Examiner alleges that in claims 19 and 22, it is unclear how the functional additive defines the region and how the functional group is related to the additive. Applicants respectfully disagree and note that, as discussed above in connection with claim 3, the functional additive defines the region in that it forms portions of the substrate surface. For instance, “[i]n a typical substrate of the invention, functional additive covers about 5% to about 60%, and more typically of about 10% to about 50% of the surface area of the substrate.” Specification, page 14, lines 6-8 and Figure 3. It is those portions of the substrate surface area covered by functional additive that are the regions defined by the functional additive. Regarding how the functional group is related to the functional additive, Applicants note that “[f]unctional additives are materials that contain functional groups to which biological and/or chemical moieties can be covalently attached.” Specification, page 10, lines 16-18. Therefore, one of ordinary skill in the art reading these phrases in claims 19 and 22 would readily understand their meaning and scope. M.P.E.P. § 2173.05(a).

The Examiner alleges that claim 23 is confusing because it does not require Formula IV to contain a surface as in claim 22. Applicants respectfully disagree. However, claim 23 has been amended to further prosecution by replacing the symbol “R” with “Surface,” and by reciting that Surface is the surface of the porous substrate. Support for this amendment can be found in the specification on page 6 line 12.

The Examiner suggests that claim 24 should be amended by inserting --X is NH₂ in-- after the “wherein” in line 1, canceling “X is NH₂” in its existing position in the claim, and inserting --the material-- after “and.” The Examiner also suggests that “R” in claim 24 should be replaced with --surface-- to be consistent with Formula III of claim 22. Applicants have amended claim 24 according to the Examiner’s suggestions. Support for this amendment can be found in the specification on page 6, lines 14-20.

The Examiner alleges that claims 28 and 30 are confusing by requiring Formulas VIII and IX to contain “R”, since Formulas VIII and IX are the formulas of the spacer. The Examiner suggests that “R” be removed from Formulas VIII and IX, and that Formulas VIII and IX of the spacer be set forth in the type of way as in claim 14 when defining a formula for the spacer of claim 13. Although Applicants respectfully submit that the claims as filed are not confusing, claims 28 and 30 have been amended to replace the “R”

with a wavy line. Support for this amendment can be found in the specification on page 20, lines 5-12.

THE REJECTION UNDER 35 U.S.C. § 102(B) SHOULD BE WITHDRAWN

Claims 3, 5-7, 9-13, 15, 19 and 20 were rejected under 35 U.S.C. § 102(b) as allegedly anticipated by U.S. Patent No. 4,855,234 to Hendrickson *et al.* ("Hendrickson") for the reasons set forth on pages 5 and 6 of the Office Action. Applicants respectfully traverse the rejection for the reasons set forth below.

As the Examiner is aware, a prior art reference must disclose all the limitations of a claim in order to anticipate the invention recited by that claim. MPEP § 2131. There must be no difference between the claimed invention and the reference disclosure as viewed by one of ordinary skill in the art. *Scripps Clinic & Research Fdn. v. Genentech*, 927 F.2d 1565, 1576 (Fed. Cir. 1991). Put another way, "[a] claim is anticipated and therefore invalid only when a single prior art reference discloses *each and every limitation of the claim*." *Glaxo Inc. v. Novapharm Ltd.*, 52 F.3d 1043, 1047, *cert. denied*, 116 S. Ct. 516 (1995) (citations omitted) (emphasis added).

The claimed invention is directed, in part, to porous polymeric substrates sintered with functional additives, to which biological or chemical moieties are bound via a spacer. Specification, page 2, lines 14-16 and page 14, lines 26-28. As amended, independent claims 3 and 19 recite a sintered, porous substrate comprised of a polymer and a functional additive, a spacer covalently bound to the region, and a chemical or biological moiety covalently or non-covalently bound to the spacer. As disclosed in the specification, preferred substrates of the invention are made by sintering a mixture comprising particles of at least one polymer and particles of a functional additive. Specification, page 14, lines 26-28. The specification also discloses that functional additives are readily incorporated into the porous substrate without degrading during the thermal process (*i.e.*, sintering). Specification, page 13, lines 20-22.

Hendrickson is directed to an article that can be used in a method for disinfecting medical devices, particularly contact lenses. (Hendrickson, col. 1, lns. 14-16). In particular, Hendrickson is directed to a composite article comprising a fibrous support, a coating solution containing inorganic oxide particles, a protein immobilizer, and a biologically active protein bound to the layer of protein immobilizer. (Hendrickson, col. 5, lns. 4-13). Preferred materials used to prepare the fibrous support include polymers, such as

polyethylene or polypropylene. (*Id.*, col. 5, lns. 46-50). While the polymeric support of Hendrickson is a woven or non-woven web, it is not a sintered, porous matrix. (Hendrickson, col. 2, lns. 42-43). Preferred inorganic oxide particles include colloidal silica particles. (*Id.*, col. 7, lns. 57-59). Suitable protein immobilizers include silane functional compounds. (*Id.*, col. 6, lns. 56-61). Biologically active proteins include enzymes, such as glucose isomerase and urease. (*Id.*, col. 7, lns. 21-33).

The Examiner alleges that the composite article and process for its preparation as disclosed by Hendrickson are the same as the material claimed in the present invention. Specifically, the Examiner alleges that the fibrous support of Hendrickson is inherently a porous polymer substrate, the silica particles are inherently a functional additive defining a surface region of the support, and the silane immobilizer is inherently a spacer.

Hendrickson clearly does not anticipate the claimed invention. In particular, Hendrickson fails to disclose a sintered, porous substrate comprised of polymer and a functional additive. The polymeric support of Hendrickson is a woven or non-woven polymeric web, not a sintered, porous matrix. (See Hendrickson, col. 2, lns. 42-43). Thus, there is a substantial inherent difference between the present invention's sintered, porous polymeric matrix and Hendrickson's fibrous support. For the above reason, Hendrickson does not anticipate the claimed invention. Applicants respectfully request that the rejection of claims 3, 5-7, 9-13, 15, 19 and 20 under § 102 be withdrawn.

THE REJECTION UNDER 35 U.S.C. § 103(A) SHOULD BE WITHDRAWN

Claim 4 was rejected under 35 U.S.C. § 103(a) as allegedly unpatentable over Hendrickson in view of U.S. Patent No. 5,773,308 to Conrad *et al.* ("Conrad") for the reasons set forth on page 6 and 7 of the Office Action. Applicants respectfully traverse this rejection.

As the Examiner is well aware, three basic criteria must be met to establish a case of *prima facie* obviousness: first, there must have been at the time of the invention a motivation to combine the references cited; second, the alleged prior art must teach or suggest all of the limitations of the claims alleged to be obvious; and third, there must have been at the time of the invention a reasonable expectation of success. MPEP § 2142. Furthermore, hindsight cannot be used to reject a claim as obvious. MPEP § 2141.01. Consequently, when determining whether or not a claimed invention is obvious, one must cast his "mind back to the time of invention, to consider the thinking of one of ordinary skill in the art, guided only by the prior art references and the then-accepted wisdom in the field."

In re Dembiczak, 175 F.3d 994, 999 (Fed.Cir. 1999) (reversing a determination that several claims were obvious over a combination of references that disclosed all of their limitations, but which did not provide a motivation to combine those limitations).

Conrad is directed to compounds and methods used in immunoassay analytical techniques so that a plurality of bioassays can be conducted simultaneously. (Conrad, col. 1, lns. 9-12 and lns. 25-27). Conrad discloses producing patterned arrays using photoactivable O-nitrobenzyl polyethylene glycol-silane attached to a substrate. (Conrad, col. 2, ln. 63-col. 3, ln. 34). The substrate containing the silane is irradiated through a mask that blocks certain regions of the substrate from being irradiated to result in only certain regions being photoactivated for attachment of an anti-ligand such as an enzyme or antibody. *Id.* The Examiner alleges that it would have been obvious to use the photoactivable O-nitrobenzyl polyethylene glycol-silane of Conrad as the silane immobilizer of Hendrickson to form the patterned surface suggested by Conrad.

Claim 4 recites the sintered, porous substrate of claim 3 in which the surface comprises a plurality of regions defined by at least some of the functional additive. This claim is not rendered obvious by Hendrickson in view of Conrad. As previously discussed, Hendrickson does not teach or suggest all of the limitations of amended claim 3 of the present invention, from which claim 4 depends. Conrad does nothing to resolve this deficiency in Hendrickson. Conrad merely teaches a patterned array that can be produced using photoactivable O-nitrobenzyl polyethylene glycol-silane attached to a substrate. (Conrad, col. 2, ln. 63-col. 3, ln. 34). The pattern is produced by using a mask to block certain regions of the substrate from being irradiated. *Id.* Conrad does not disclose or suggest use of a sintered, porous polymeric substrate. Accordingly, Hendrickson in view of Conrad does not teach or suggest all of the limitations of claim 4, and thus does not render claim 4 obvious. For these reasons, Applicants respectfully request that the rejection of claim 4 under 35 U.S.C. § 103(a) be withdrawn.

Claims 8 and 21 were rejected under 35 U.S.C. § 103(a) as allegedly unpatentable over Hendrickson in view of U.S. Patent No. 6,524,489 to Palm *et al.* ("Palm") for the reasons set forth on page 7-8 of the Office action. Applicants respectfully traverse this rejection.

Palm is directed to composite filtration media. (Palm, col. 1, lns. 11-14). Palm discloses composite filtration media prepared by blending a functional filtration component, such as silica, with a matrix component, such as polyether ketone (PEEK), and sintering to cause agglomeration. (Palm, col. 1, lns. 11-25; col. 7, ln. 9; and col. 11, ln. 4).

The Examiner alleges that it would have been obvious to form the composite article of Hendrickson by sintering and using PEEK as a matrix component as taught by Palm.

Claim 8 ultimately depends from claim 3 and recites that the polymer is PEEK. Claim 21 depends from claim 19 and recites that the porous substrate is formed by sintering beads and then attaching the spacer, or attaching the spacer to beads prior to sintering the beads. Neither claim 8 nor claim 21 is rendered obvious by Hendrickson in view of Palm, in part because there would have been no motivation to combine Palm and Hendrickson. MPEP § 2142. Hendrickson discloses an article used in a method for disinfecting medical devices, particularly contact lenses. (Hendrickson, col. 1, lns. 13-15). Palm relates to a filtration media used in filtration applications. (Palm, col. 1, lns. 11-14). Thus, the two references are in different fields of art. Not only are the two fields of art different, but the two articles produced by the two references are also vastly different. The polymeric composite article of Hendrickson with its layer of protein immobilizer attached to a biologically active protein is a vastly different product than the composite filtration media of Palm. Applicants submit that there would be no teaching, suggestion or motivation to combine these two disparate references, as medical device disinfection and media filtration are in two completely different fields of art. M.P.E.P. § 2142. Moreover, given both the different fields of art and the different products produced by the two references, Applicants respectfully submit that this combination of references evidences the use of improper hindsight reconstruction. M.P.E.P. § 2141.01(a), citing *In re re Dembiczak*, 175 F.3d 994, 999 (Fed.Cir. 1999) (reversing a determination that several claims were obvious over a combination of references that disclosed all of their limitations, but which did not provide a motivation to combine those limitations). For the above reasons, Hendrickson in view of Palm does not render claims 8 and 21 obvious.

Claims 14, 22-25 and 28-30 were rejected under 35 U.S.C. § 103(a) as allegedly unpatentable over Hendrickson in view of U.S. Patent No. 4,897,468 to Oka *et al.* (“Oka”) or U.S. Patent No. 4,384,045 to Ho *et al.* (“Ho”), and further in view of U.S. Patent No. 6,004,786 to Yamashita *et al.* (“Yamashita”) for the reasons set forth on page 8 of the Office Action.

Oka is directed to a bioreactor which comprises immobilizing a peptide-containing compound to a specific carrier. (Oka, col. 1, lns. 14-19). Oka discloses a process for preparing a bioreactor, which comprises hydrolyzing a metal alkoxide, such as $\text{Si}(\text{OCH}_3)_4$. (Oka, col.1, lns. 60-68; col. 2, lns. 26-36).

Ho is directed to the preparation of a siliceous carrier for use in preparation of multi-layered immobilized enzymes. (Ho, col. 1, lns. 14-18). Ho discloses a process for activating a siliceous carrier to which a biologically active material, especially an enzyme, can allegedly be coupled. (Ho, col. 1, lns. 11-17).

Yamashita is directed to enzyme immobilizing carriers and immobilized lipase used as a bioreactor. (Yamashita, col. 1, lns. 8-12). Yamashita discloses an inorganic carrier produced by combining the inorganic carrier with a silane coupling agent having carboxylic-ester linkage. (Yamashita, col. 2, lns. 33-41).

The Examiner alleges that Oka, Ho, and Yamashita disclose the type of silanes required as a coupling agent for immobilizing an enzyme on a carrier. The Examiner alleges that it would have been obvious to use as the silane of Hendrickson a silane of the type taught by Oka, Ho, or Yamashita, since these silanes would have been expected to provide the function of a silane as disclosed by Hendrickson.

Claims 23-25 and 29 ultimately depend from independent claim 22, and claims 14, 28 and 30 ultimately depend from claim 3. As amended, claim 22 recites a method of providing a material which comprises forming a sintered, porous substrate similar to that in previously discussed claim 3, but which contains a particular spacer compound which bonds to a hydroxyl group on the surface of the substrate. Neither claim 3 nor claim 22 is rendered obvious by Hendrickson in view of Oka, Ho, or Yamashita for several reasons.

First, the combination of so many references from different fields of art is strong evidence against the existence of a *prima facie* case of obviousness. In this rejection, the Examiner is combining four references. M.P.E.P. § 2142. Although reliance on a large number of references in a rejection does not itself weigh against the obviousness of the claimed invention, “[i]t is still impermissible . . . to engage in a hindsight reconstruction of the claimed invention.” *In re Gorman*, 933 F.2d 982, 986 (Fed. Cir. 1991) (citing *Interconnect Planning*, 774 F.2d at 1143 (Fed. Cir. 1985)). In *Gorman*, the Federal Circuit affirmed a rejection of a claim to a candy sucker shaped like a thumb on a stick based on thirteen prior art references, all of which were concerned closely related candy and ice cream molding inventions. *Id.* at 985-86. Here, the reliance on four references suggests hindsight reconstruction, in part because the references themselves do not provide a suggestion to combine the elements of the various teachings to make the applicant’s invention. As previously discussed, Hendrickson relates to an article used in a method for disinfecting medical devices, particularly contact lenses. (Hendrickson, col. 1, lns. 13-15). Oka, however, relates to a bioreactor suited for use of analysis, diagnosis, and synthesis. (Oka, col. 1, lns.

14-19). Yamashita relates to enzyme immobilizing carriers and immobilized lipase used also as a bioreactor. (Yamashita, col. 1, lns. 8-11). Ho relates to the preparation of a siliceous carrier for use in preparation of a multi-layered immobilized enzyme composite. (Ho, col. 1, lns. 14-17). Given the disparity in subject matter between these references, one of ordinary skill in the art would not have been motivated to combine these references to arrive at the present invention. The difference in subject matter between Hendrickson and Oka, Yamashita or Ho is much greater than that in the references in *Gorman*, which all related to candy molding. Therefore, the combination of so many disparate references as a basis for an obviousness rejection weighs against the obviousness of the claimed invention.

Second, as with independent claim 3, Hendrickson does not disclose or suggest each and every limitation of claim 22. Hendrickson does not disclose or suggest a sintered, porous polymeric substrate in which a functional additive is incorporated. None of Oka, Ho, or Yamashita resolve this deficiency. None disclose a sintered, porous polymeric substrate, much less a sintered, porous polymeric substrate with a functional additive. Accordingly, these references, either alone or in combination with Hendrickson, do not render claims 14, 22-25 and 28-30 obvious.

Claims 16, 17 and 18 were rejected under 35 U.S.C. § 103(a) as allegedly unpatentable over Hendrickson, Oka, Ho and Yamashita, and further in view of U.S. Patent No. 5,552,325 to Nochumson *et al.* ("Nochumson") for the reasons set forth on pages 8-9 of the Office Action. Applicants respectfully traverse this rejection.

Nochumson is directed to a centrifuge tube for separating and recovering biological substances from liquids. (Nochumson, col. 1, lines 10-23). Nochumson discloses a device for selective binding of a biological material such as DNA. (Nochumson, col. 1, lns. 10-23). The device contains a microporous resinous matrix having particulate binding sites dispersed throughout. (*Id.*, col. 8, lns. 48-67). The dispersed particulate may be silica, and the matrix may be made of polyethylene or polypropylene. (*Id.*, col. 9, lns. 16-37; col. 8, lns. 39-40). The Examiner alleges that when forming the composite of Hendrickson with a silane of the type taught by Oka, Ho, or Yamashita, it would have been obvious to disperse the silica particulate within the support as suggested by Nochumson, since having the silica embedded in the support would make the silica more resistant to removal from the support.

As amended, claim 16 and 17 recite a material comprising a sintered, porous polyethylene substrate having a surface in which a functional additive is embedded, and a spacer of a specific formula covalently attached to a portion of the functional additive. In claim 17, the spacer is further covalently attached to a biological or chemical moiety. Claim

18, which depends from claim 17, lists specific chemical or biological moieties. Claims 16 - 18 are not rendered obvious by the above combination of references for several reasons.

First, as discussed above, the combination of so many references from different fields of art is strong evidence against the existence of a *prima facie* case of obviousness. M.P.E.P. § 2142. In this rejection, the Examiner is combining five references. Nochumson relates to a centrifuge tube for separating and recovering biological substances from liquids. (Nochumson, col. 1, lns. 10-23). Given the disparity in subject matter between Nochumson and the four references discussed above, it is doubtful that one of ordinary skill in the art would be motivated to combine this prior art to arrive at the present invention. Therefore, the combination of so many disparate references as a basis for an obviousness rejection weighs against the obviousness of the claimed invention.

Additionally, Applicants respectfully submit that the combination of references does not teach or suggest every limitations of claims 16-18. Hendrickson neither discloses nor suggests each and every element of independent claims 16 and 17 and dependent claim 18. More specifically, Hendrickson does not disclose or suggest a sintered, porous polymeric matrix in which a functional additive is either integrally bound or embedded. None of Oka, Ho, or Yamashita resolve this deficiency. None disclose a sintered, porous polymeric substrate much less a sintered, porous polymeric substrate with a functional additive. Nor does Nochumson resolve this aspect of the invention, as it does not disclose a sintered, porous polymeric substrate. By not disclosing or suggesting each and every limitation of claims 16-18, the above prior art further in view of Nochumson does not render these claims *prima facie* obvious. For the above reasons, Applicants respectfully submit that the claimed invention is not obvious, and request that the rejection of claims 16-18 under § 103 be withdrawn.

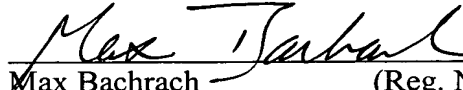
CONCLUSION

Applicants believe the application is in condition for allowance and request reconsideration of the claims and allowance thereof. If the Examiner has any questions or suggestions to expedite allowance of this application, however, the Examiner is respectfully invited to call the undersigned to discuss the matter further.

No fee is believed to be due for this submission. Should any fee be required, however, please charge such fee to Pennie & Edmonds LLP Deposit Account No. 16-1150.

Respectfully submitted,

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